NIH-RAID: A ROADMAP Program

(Rapid Access to Interventional Development)

A Program designed to facilitate the development of new therapeutics
The NIH–RAID Pilot Program

- The NIH-RAID Pilot Program is intended to reduce some of the common barriers between laboratory discoveries and clinical trials for new therapies

- The NIH-RAID Pilot Program provides services to approved projects through access to the extensive NCI contract network

  - Eligible projects can span the spectrum of human disease, and may be supported by multiple Institutes
The Valley of Death

- University proof of concept
- NIH Roadmap – Approaches to Translational Research
- Compound in the clinic
The Added Value of Translational Research can help academia enlist corporate support

- Scale up synthesis
- Pharmacokinetics
- Toxicology
- IND

Industry or NIH - supported Clinical Trials
Translational Research Core Resources: NIH RAID Pilot

Provides resources not readily available to academic & non-profit investigators to small businesses; fills gaps in translational pipeline

Complements and facilitates private sector infrastructure and support.
NIH–RAID Overview

Not a grant mechanism; service provided

Investigator initiated; peer reviewed by CSR

Intellectual property and project control remains with originating institution and investigator

Focus is on small molecules or natural products, but certain biologicals can be considered

Projects are conducted by current NCI contractors, with the exception of vector manufacture, which is done through the NHLBI Gene Therapy Research Program
ELIGIBILITY

Intended for use by academic discovery laboratories, not-for-profit organizations, and SBIR-eligible companies.

Domestic and foreign institutions are eligible

Partnerships with non-small business entities can be critical in the development process: products may be licensed to corporate partners and still be eligible for RAID
NIH-RAID Pilot Services

- Synthesis of small molecules and oligos, chemical synthesis of small peptides (GMP and non-GMP)
- Scale-up production to clinical-trials lot scale
- Development of analytical methods for bulk substances
- Isolation, purification of active entities from natural sources
- Development of pharmacology assays and conduct of pharmacologic studies
NIH–RAID Pilot Services, cont.

- Development of suitable formulations
- Characterization of formulations
- Range-finding initial toxicology
- IND-directed toxicology
- Product development planning and advice in IND preparation
Recently Announced New NIH-RAID Pilot Services

- The NIH-RAID Pilot will consider: Requests for manufacture of material for any clinical study.
- Services to support later-stage preclinical development of monoclonal antibodies, recombinant proteins, and gene therapy agents.
- Manufacture of non-GMP viral and non-viral gene vectors as well as GMP-grade adeno-associated virus and lentivirus vectors.
- Synthesis of monoclonal antibodies or recombinant proteins will not be considered.

NIH Guide Notice NOT-RM-08-025
NIH-RAID Administrative Supplements for Preclinical Efficacy Testing of Candidate Therapeutics

Intent: to facilitate the development of novel therapeutic agents by providing funds for in vitro or in vivo efficacy assessment

Administrative supplements can be requested for active Research Projects of a variety of types, including SBIR grants, if the grant has at least one year of funding remaining.

The research proposed in the supplement request must be within the original scope of the NIH-supported grant project.

Requesters are strongly advised to discuss their plans with the NIH Program Officer who oversees the parent grant.

Applications are received electronically through Grants.gov.

- The NIH-RAID Pilot Program uses the NIH Resource Access (X01) award mechanism.

- Three receipt dates per year are announced.

- Applicants are allowed an initial submission and one resubmission.
Review Criteria

- Development should represent a significant advance over currently available therapy or address an unmet medical need

- Existing data should provide compelling support for the efficacy of the candidate therapeutic?

- The requested NIH-RAID Pilot services may significantly advance the candidate therapeutic toward a Phase I clinical trial

- Plans and resources are available to complete the tasks required for IND submission if those services are not requested

- Appropriate plans are in place and potential resources identified to initiate clinical testing of the candidate therapeutic

- Are there any intellectual property or patent issues that could hinder the development and/or marketability of the candidate therapeutic?
## 2009\2010 Application Receipt Dates

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Letter of Intent Deadline</th>
<th>Application Deadline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cycle 13</td>
<td>August 17, 2009</td>
<td>September 15, 2009</td>
</tr>
<tr>
<td>Cycle 14</td>
<td>December 16, 2009</td>
<td>January 15, 2010</td>
</tr>
<tr>
<td>Cycle 15</td>
<td>April 14, 2010</td>
<td>May 14, 2010</td>
</tr>
<tr>
<td>Cycle 16</td>
<td>August 16, 2010</td>
<td>September 15, 2010</td>
</tr>
</tbody>
</table>
INVESTIGATOR

Stage I - Administrative assessment

Stage II – CSR Peer Review

Decision on Seminar Invitation

IC/Roadmap-Funding decision

Access to Resources
Internal NIH considerations

All submissions will be assigned to NINDS for administration, and to a Special Emphasis review panel (SEP)

Proposals are discussed and scored by the SEP

After the review, a tentative cost analysis is performed by NCI program staff

Reviews and cost analyses are transmitted to staff of the Institute(s) that have a mission related to the project

A decision is made by Institute staff as to whether an invitation to give a seminar should be offered

At the seminar, the investigator(s) describe the project’s status, Institute and RAID staff ask questions, and consensus is reached on what RAID will support and milestones to be set.

Final costs are developed and funding decision made
Typical project plan and cost assessment

### Example - Preclinical toxicity
Candidate Drug Analogs, p.o.

<table>
<thead>
<tr>
<th>Task</th>
<th>1Q06</th>
<th>2Q06</th>
<th>3Q06</th>
<th>4Q06</th>
<th>1Q07</th>
<th>2Q07</th>
<th>3Q07</th>
<th>4Q07</th>
<th>1Q08</th>
<th>2Q08</th>
<th>3Q08</th>
<th>4Q08</th>
</tr>
</thead>
<tbody>
<tr>
<td>IP Status (confirm w/PI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>non-GMP Synthesis (3 cmps x 25-50 g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-formulation (3 cmps x 2 g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efficacy * (3 cmps x 5 g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$50K</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PK (3 cmps x 2 g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early Genotox Screen (4 cmp)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full Genotox (1 cmp x 5 g)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GMP Synthesis (1 cmp, 2-3 Kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range-finding Tox inc methods (1 cmp, 0.5-1 Kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IND Tox (1 cmp, 90 day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$700K, &gt;&gt;&gt; 1Q09</td>
</tr>
<tr>
<td>Phase 1 Drug Supply (1 cmp)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$100K, &gt;&gt;&gt; 1Q09</td>
</tr>
</tbody>
</table>

*Cost Estimate: $2.14 MM  
Time Estimate: 3.0 yrs

*to be performed by PI; TBD = cost to be determined after initial synthesis

03/06/06
Examples of Approved Projects

- Development of HGF Mimetic (Refanalin) for Hepatic Fibrosis
- IND-enabling toxicology and safety pharmacology studies of ATN-161 for the treatment of Crohn’s disease
- Safety Pharmacology Studies for an IND for Beta Thalassemia
- Metastin Administration in Humans: Preclinical Toxicology Studies
- Redox Encrypted Therapeutics for Treatment of Friedreich’s Ataxia
- Advanced Studies with 5HMF –Potent Antisickling Agent
- Preclinical Development of CDD-0102 Treatment of Alzheimer’s disease
- A Potent Oral Therapy for Cytomegalovirus Infection
Type 1 Diabetes-Rapid Access to Intervention Development

A collaborative effort between NI DDK and NCI

Program Administrator:
Myrlene Staten, MD, Senior Advisor, Diabetes Research Translation, NI DDK
(301) 402-7886
statenm@mail.nih.gov
Eligibility for T1D RAI D

- Academic Institutions
- Non-profit research institutions
- Biotechnology and pharmaceutical companies
- U.S. and non-U.S. entities

Available Resources - Similar to NIH-RAID

Submission dates - April 1 and Nov 1

Review by external experts
NINDS (National Institute of Neurological Disorders and Stroke) Translation Initiatives

- Exploratory/Developmental Projects (R21) - intended to complete preliminary steps for pre-clinical development of therapeutics for neurological or neuromuscular disorders
- Full-scale single-component research projects (U01)
- Full-scale multi-component research projects (U54)
- Small Business Awards (SBIR [U44])
- Translational Research Resource Centers (U24): national resources to support investigators engaged in therapy development for neurological disorders

http://www.ninds.nih.gov/research/translational/Coop_Tran_Res.htm
NCI (National Cancer Institute)

- **NCI RAID – for Academics**: to provide clinical proof of principle that a new molecule or approach is a viable candidate for expanded clinical evaluation. Tasks supported are similar to those for NIH–RAID. Products returned to the originating investigator.

- Academic researchers may submit applications twice yearly—February 1 and August 1.

- **Drug Development Group — for Academics and Industry**
  Meets monthly to consider developing drugs from discoveries in the NCI intramural and extramural academic communities, as well as with the pharmaceutical industry.

- Preclinical development is done by NCI

  [dctd.cancer.gov/ProgramPages/dtp/major_drug_development.htm](http://dctd.cancer.gov/ProgramPages/dtp/major_drug_development.htm)
National Institute of Mental Health (NIMH)

- Molecular Pharmacology Research Program Resources
- Psychoactive Drug Screening—screening for activity at CNS receptors, channels, and transporters. Assays available for bioavailability and cardiovascular toxicity
- Chemical Synthesis and Drug Program—synthesizes and distributes novel research chemicals, psychoactive drugs, and candidates for therapeutics

Contact: Jamie Driscoll
- drisco1@mail.nih.gov
National Heart, Lung, and Blood Institute (NHLBI) Gene Therapy Resource Program

- Facilitates translation of gene therapy research into clinical interventions
- Provides resources primarily to heart, lung, and blood investigators, but other requests may be considered
- Preclinical & clinical grade vectors, pharm/tox, clinical trial funds and regulatory support
- Submission Sept. 15 & Feb. 15
- www.gtrp.org
The Division of AIDS (DAIDS) offers contract resources to assist HIV/AIDS investigators in the preclinical development and evaluation of new therapies and microbicides. 
In vitro & in vivo testing, synthesis, analytical chemistry, formulation, manufacture, pharm/tox
www.niaid.nih.gov/daids/pdatguide/request.htm

The Division of Microbiology and Infectious Diseases (DMID) offers a collection of preclinical services to support the development of promising therapeutic candidates, including biodefense.
www3.niaid.nih.gov/LabsAndResources/resources/dmid/pretheraagents
IND Toxicology Program (Services only)
- To identify new therapeutics for Alzheimer’s and other conditions associated with aging
- Contact buckholn@gw.nia.nih.gov

Drug Discovery Announcement
- Alzheimer’s Disease Drug Development Program (U01)
- Testing new therapeutics for age-related cognitive decline
  grants.nih.gov/grants/guide/pa-files/PAR-08-266.html
Medications Development Program
  ◦ Contract services for preclinical and clinical development for IND- and NDA-directed drug development projects for the treatment of drug addiction disorders
  ◦ Grants and contracts for Phase I through III clinical testing
  ◦ dmccann@mail.nih.gov
Summary – NIH offers access to resources

The Roadmap and other such translational activities are aimed at adding value by assisting with early-stage drug development.

Good regulatory and business advice is provided to develop a workable product development plan.

With preclinical data and an IND plan, the academic or small business investigator is in a position to interest venture capital and/or the biotech and pharmaceutical industry.